DANA-FARBER CANCER INSTITUTE

St. Elizabeth's Medical Center
A STEWARD FAMILY HOSPITAL
Steward

IRB APPROVED
AS MODIFIED
Feb 22, 2023

RESEARCH SUBJECT CONSENT FORM

Title: Improving Quality of Life of Prostate Cancer Survivors with Androgen Deficiency

Protocol No.: DFCI Protocol # 18-733
WCG IRB Protocol #20182169

Sponsor: NIH (NIA)

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Clinical Research and Study Coordinators
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617-732-6660

Summary

You are being asked to take part in this research study because you have a history of prostate cancer and because you have undergone radical prostatectomy for your cancer. This research

study is looking at whether testosterone replacement therapy improves quality of life for men who've undergone prostate removal for prostate cancer and have very low probability of recurrent disease.

If you are found eligible and agree to enroll in the study, you will be asked to attend 15-19 study visits at the Brigham and Women's hospital over a period of approximately 6-8 months. At these visits, you'll undergo various clinical procedures including blood draws, physical exams, DXA scans, and physical function tests. You will receive weekly injections of testosterone or placebo for a 12-week period during the study. Your health will be closely monitored by study clinicians, and you will be financially compensated for each study visit you complete.

What should I know about this research?

- Someone will explain this research to you.
- This form sums up that explanation.
- Taking part in this research is voluntary. Whether you take part is up to you.
- You can choose not to take part. There will be no penalty or loss of benefits to which you are otherwise entitled.
- You can agree to take part and later change your mind. There will be no penalty or loss of benefits to which you are otherwise entitled.
- If you don't understand, ask questions.
- Ask all the questions you want before you decide.

Why is this research being done?

The purpose of this research is to evaluate the safety and efficacy of testosterone replacement therapy in men aged 40 and older, who have undergone prostate removal for prostate cancer and have very low probability of recurrent disease. Investigators are studying whether testosterone replacement therapy is beneficial and safe in improving sexual function, health related quality of life, muscle mass and muscle strength. The use of testosterone in the study is considered experimental.

This research study will compare testosterone to placebo. The placebo looks exactly like testosterone but contains no testosterone. During this study, you may get placebo instead of testosterone. Placebos are used in research studies to see if the results are due to the study drug or due to other reasons.

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

It is expected that about 500 men will screen in this study at three recruitment sites.

How long will I be in this research?

It will take you up to 8 months to complete this research study. During this time, we will ask you to complete 15-19 study visits. The first visit, an in-person screening visit, may take place at either Brigham and Women's Hospital or St. Elizabeth's Medical Center in Boston. Eligible subjects who decide to enroll will complete all additional study visits at our research clinic at Brigham and Women's Hospital (BWH) with the opportunity to conduct some weekly procedures at the Multi-Specialty Clinic in Foxboro, MA.

For subjects who express interest in participating but are not willing to travel to BWH for weekly injections, a study clinician (RN, NP, or MD) will visit the subject's house to conduct study procedures such as blood draws, weekly injections, and administering questionnaires. The goal is for a clinician to conduct some study procedures during these home visits or at an IRB approved research locations to reduce subject burden of traveling to Boston on a weekly basis.

The clinicians will not be doing any of the exercise assessments because it will be too difficult to perform the procedures without the proper equipment. Therefore, some screening procedures, Baseline, Week 6, and Week 12/Early termination visit will need to occur in the clinic.

What happens to me if I agree to take part in this research?

If you choose to take part in this study, we will ask you to sign this consent form before we do any study procedures. Participation in the study will include the following:

Before the Research Starts: Screening Procedures

We will ask you to arrive in a fasting state (fasting for at least 8 hours). If you decide to sign this consent form and move forward with eligibility screening, the procedures listed below will take place. The screening procedures may be spread over 2 trips to the clinic. This visit will take about 2 hours.

- We'll ask you about your medical history and medications
- Physical exam
- Vital signs, height, and body weight
- Blood collection
- EKG
- Questionnaires to assess fatigue, mood, and sexual desire and function

Before the Study Treatment begins: Baseline Assessments

If you are found eligible and decide to participate, we'll ask you to complete the baseline procedures listed below. These visit procedures may be spread over 2-3 trips to the clinic. It will take 4-6 hours total to complete all the Baseline procedures.

Baseline procedures will occur within 2 weeks of your first dose of study medication.

- Blood draw (fasting for 8 hours)
- EKG (if not completed during screening visit)
- We'll ask you about any changes to your health or medications since your last visit
- Questionnaires to assess fatigue, mood, sexual desire and function, cognition and physical fitness
- Whole body DXA (bone density) scan
- Exercise testing to measure strength, aerobic capacity, physical function, and remote gait speed

Randomization: (Day 0)
Randomization will occur on the last day of your Baseline procedures. At this visit, you will be "randomized" to one of two study groups: the testosterone group or the placebo group (placebo looks exactly like testosterone but contains no medicine). Randomization means that you are put into a group by chance, like drawing numbers from a hat. Neither you nor the research doctor will choose or know what group you will be in. You will have a 50% chance of being assigned to the testosterone group. You will receive your first injection of study medication (testosterone or placebo) at this visit.

Weekly Injection Visits: Weeks 1-5
These visits will take about 30 minutes to 1 hour.

- We'll ask about any changes to your health or medications since your last visit
- Administration of study drug
- Weeks 2 and 4 only - Blood draw (fasting for 8 hours)

Weekly Injection Visits: Week 6 (Mid-point Assessments)
This visit will take about 1 hour.

- We'll ask you about any changes to your health or medications since your last visit
- Blood draw (fasting for 8 hours)
- Urinalysis
- Physical Exam
- Vital signs and weight
- Questionnaires to assess fatigue, mood, sexual desire and function, and physical fitness
- Administration of study drug

Weekly Injection Visits: Weeks 7-11
These visits will take about 30 minutes to 1 hour.

- We'll ask you about changes to your health or medications since your last visit
- Administration of study drug
- Week 8 only- Blood draw (fasting for 8 hours)

Weekly Injection Visits: Week 12 (End-of-Study Assessments)
These visit procedures may be spread over 2-3 trips to the clinic. It will take 4-6 hours to complete all the End of Study procedures.

- We'll ask you about any changes to your health or medications since your last visit
- Physical exam
- Vital signs and weight
- Blood draw (fasting for 8 hours)
- Questionnaires to assess fatigue, mood, sexual desire and function, cognition, and physical fitness
- Whole body DXA scan
- Exercise testing to measure strength, aerobic capacity, physical function, and remote gait speed
- Administration of study drug

3-Month Follow-up
This visit will take place approximately 3 months after your last injection of study drug.

- We'll ask you about any changes to your health or medications since your last visit
- Blood draw (fasting for 8 hours)

The total amount of blood collected from each study participant is approximately 127 mL. This is about 8 tablespoons over the course of all the visits.

Note: In the event that a planned procedure can't be completed during a visit (e.g equipment malfunction, poor image quality on DXA scans, or other unforeseen circumstances), participants may be asked to return to the clinic for an additional visit for repeat testing.

What are the risks of being in this research study?

Risks of Blood Drawing
The risks of blood drawing include pain, bleeding, and/or a bruise where the needle was inserted. Serious complications such as blood clots or infection are very rare when proper precautions are taken.

Exercise Assessments (Aerobic Capacity and Muscle Strength)
As with any exercise, there are potential health risks; however, we will take measures to minimize these risks. The risks associated with the physical function testing are minimal and include: 1) muscle soreness or strain; 2) a small possibility of loss of balance or fall; and 3) a very small possibility of angina (chest pain) from overexertion.

Potential risks of these assessments will be prevented or minimized by several safety measures. All tests will be administered by well-trained and experienced exercise physiologists using standardized procedures.

Risks of Testosterone Administration in Prostate Cancer Survivors

Testosterone therapy can result in some side effects such as acne, oiliness of skin and breast tenderness. The frequency of breast enlargement has been low in studies of testosterone treatment in men with low testosterone. Increase in red cell count is the most frequent side effect reported in studies of testosterone, but you will be watched very closely with frequent red cell count measurement.

We do not know for sure whether testosterone treatment increases the risk of cardiovascular disease. The largest study of 790 older men with low testosterone that were either given testosterone replacement or placebo for 12 months did not show increased cardiovascular events in men who were given testosterone. Similarly, a 36-month study of testosterone replacement or placebo also did not show worsening of atherosclerosis in men.

In men who have an intact prostate and no history of prostate cancer, the relationship between testosterone administration and the risk of prostate cancer remains poorly understood. No trial has been long enough or large enough to determine whether testosterone administration increases the risk of prostate cancer. There are no large trials of testosterone replacement therapy in prostate cancer survivors. Some small studies of testosterone have been conducted in men with localized prostate cancer. These studies have not shown evidence of an increased risk of recurrence in men with a history of low-grade, organ-confined prostate cancer. In one population-based observational study of 1181 men, testosterone therapy in prostate cancer survivors was not associated with an increased mortality. This study will be the largest study of prostate cancer survivors receiving testosterone therapy. We will monitor PSA levels very closely throughout the study.

Potential Risks of DXA Scanning

The radiation exposure during a DXA scan is minimal (less than 25 mrems, less than that from a chest X ray). While we do not know whether any dose of radiation is completely safe, the amount of radiation you will be exposed to during the study is well within the limits considered "safe" by federal and state regulations.

Potential Risks of Questionnaires

The questionnaires include questions about sexual function, mood, and health-related quality of life. You may find some of these questions embarrassing. Although we encourage subjects to answer all the questions, you have the option of not answering any or all the questions that you do not want to answer. All the questionnaires are coded, and confidentiality will be maintained using systematic data processing methods.

Will being in this research benefit me?

There are no benefits to you from your taking part in this research. We cannot promise any benefits to others from your taking part in this research. However, the information investigators

gain from this research could lead to the development of therapies that help men with prostate cancer.

What other choices do I have besides taking part in this research?

This research is not designed to diagnose, treat or prevent any disease. Your alternative is to not take part in the research.

Other alternatives for treatment may involve use of medications to treat erectile dysfunction such as sildenafil and/or physical therapy for muscular weakness.

What happens to the information collected for this research?

During this research, identifiable information about your health will be collected. In the rest of this section, we refer to this information simply as "health information." In general, under federal law, health information is private. However, there are exceptions to this rule, and you should know who may be able to see, use, and share your health information for research and why they may need to do so.

Who may see, use, and share your identifiable health information and why they may need to do so:

- Mass General Brigham and St. Elizabeth's Medical Center (SEMC) research staff involved in this study
- The sponsor(s) of this study, and the people or groups it hires to help perform this research
- Other researchers and medical centers that are part of this study and their ethics boards
- A group that oversees the data (study information) and safety of this research
- Non-research staff within Mass General Brigham and SEMC who need this information to do their jobs (such as for treatment, payment (billing), or health care operations)
- The Mass General Brigham and SEMC ethics board that oversees the research and the Mass General Brigham or SEMC research quality improvement programs.
- People from organizations that provide independent accreditation and oversight of hospitals and research
- People or groups that we hire to do work for us, such as data storage companies, insurers, and lawyers
- Federal and state agencies (such as the Food and Drug Administration, the Department of Health and Human Services, the National Institutes of Health, and other US or foreign government bodies that oversee or review research)
- Public health and safety authorities (for example, if we learn information that could mean harm to you or others, we may need to report this, as required by law)

We protect your information from disclosure to others to the extent required by law. We cannot promise complete secrecy.

We may publish the results of this research. However, we will keep your name and other identifying information confidential.

A copy of this consent form will be placed in your medical record. Medical information collected during this study and the results of any test or procedure that may affect your medical care may be included in your medical record.

Certificate of Confidentiality
In this research study, we have obtained a Certificate of Confidentiality from the Department of Health and Human Services (DHHS). By granting the Certificate, DHHS is not approving the research itself, but is helping us strengthen the privacy protections for your health information and other identifying information from the research. With the Certificate, we cannot be forced (for example by court order or subpoena) to disclose your health information or other identifying information from the research in any Federal, State or local civil, criminal, administrative, legislative, or other proceedings. (Note that information that is not from the research, such as existing hospital or office health records, is protected by general privacy law but does not receive the Certificate's stronger protection. The Certificate also does not prevent you or a member of your family from voluntarily releasing any information about yourself or your involvement in this research study.)

DF/HCC & SEMC Privacy of protected health information

Federal law requires Dana-Farber/Harvard Cancer Center (DF/HCC), St. Elizabeth's Medical Center (SEMC) and its affiliated research doctors, health care providers, and physician network to protect the privacy of information that identifies you and relates to your past, present, and future physical and mental health conditions ("protected health information"). If you enroll in this research study, your "protected health information" will be used and shared with others as explained below. If you do not sign this authorization, you cannot participate in the research.

1. **What protected health information about me will be used or shared with others during this research?**

   - Existing medical records, including mental health records.
   - New health information created from study-related tests, procedures, visits, and/or questionnaires

2. Why will protected information about me be used or shared with others?

The main reasons include the following:

- To conduct and oversee the research described earlier in this form;
- To ensure the research meets legal, institutional, and accreditation requirements;
- To conduct public health activities (including reporting of adverse events or situations where you or others may be at risk of harm); and
- To provide the study sponsor with information arising from an adverse event or other event that relates to the safety or toxicity of the drug for the purpose of this or other research relating the study drug and its use in cancer.
- Other reasons may include for treatment, payment, or health care operations. For example, some medical information produced by this research study may become part of your hospital medical record because the information may be necessary for your medical care. (You will also be given a notice for use and sharing of protected health information.)

3. Who will use or share protected health information about me?

- DF/HCC, SEMC and its affiliated research doctors and entities participating in the research will use and share your protected health information. In addition, other DF/HCC or SEMC offices that deal with research oversight, billing or quality assurance will be able to use and share your protected health information.

4. With whom outside of DF/HCC or SEMC may my protected health information be shared?

While all reasonable efforts will be made to protect the confidentiality of your protected health information, it may also be shared with the following entities:

- Outside individuals or entities that have a need to access this information to perform functions relating to the conduct of this research such as analysis by outside laboratories on behalf of DF/HCC or SEMC and its affiliates (for example, data storage companies, insurers, or legal advisors)
- The sponsor(s) of the study, its subcontractors, and its agent(s): Brigham and Women's Hospital
- Other research doctors and medical centers participating in this research.
- Federal and state agencies (for example, the Department of Health and Human Services, the Food and Drug Administration, the National Institutes of Health, and/or the Office for Human Research Protections), or other domestic or foreign government bodies if required by law and/or necessary for oversight purposes. A qualified representative of the FDA and the National Cancer Institute may review your medical records
- Hospital accrediting agencies
- A data safety monitoring board organized to oversee this research, if applicable
- Institutional Review Board

Some who may receive your protected health information may not have to satisfy the privacy rules and requirements. They, in fact, may share your information with others without your permission.

5. For how long will protected health information about me be used or shared with others?

- There is no scheduled date at which your protected health information that is being used or shared for this research will be destroyed, because research is an ongoing process.

6. Statement of privacy rights:

- You have the right to withdraw your permission for the research doctors at SEMC and participating DF/HCC entities to use or share your protected health information. We will not be able to withdraw all the information that already has been used or shared with others to carry out related activities such as oversight, or that is needed to ensure quality of the study. To withdraw your permission, you must do so in writing by contacting the researcher listed above in the section: "DF/HCC Investigator Contact Information"
- You have the right to request access to your protected health information that is used or shared during this research and that is related to your treatment or payment for your treatment, but you may access this information only after the study is completed. To request this information, please contact the researcher listed above in the section: "DF/HCC Investigator Contact Information"

What if I am injured because of taking part in this research?

If you think you have been injured as a result of taking part in this research study, tell the person in charge of this research study as soon as possible. The research doctor's name and phone number are listed in this consent form.

The treating hospital will offer you the care needed to treat injuries directly resulting from taking part in this research. These treatments may be billed to your insurance company. You will be responsible for deductibles and co-payments. There are no plans to pay you or give you other compensation for the injury. You do not give up your legal rights by signing this form.

We will need to collect certain personal information about you for insurance or payment reporting purposes, such as your name, date of birth, gender, social security number or Medicare identification number and information related to this research study. We may be required to report this information to the Centers for Medicare & Medicaid Services. We will not use this information for any other purpose.

Can I be removed from this research without my approval?

The person in charge of this research can remove you from this research without your approval. Possible reasons for removal include:

- It is in your best interest
- You have a side effect that requires stopping the research
- You are unable to keep your scheduled appointments

If we remove you from the study before you finish it, we will tell you why.

What happens if I agree to be in this research, but I change my mind later?

If you take part in this research study, and decide to drop out, you should tell us. We will make sure that you stop the study safely. We will also talk to you about follow-up care, if needed.

If you decide to stop taking part in the study for any reason, we will ask you to make a final study visit. The procedures performed at this final visit would be the same as the Visit 14 (Week 12) procedures described above.

Will it cost me money to take part in this research?

Study Drugs
Testosterone or matching placebo will be provided at no cost to you while you are participating in this study.

Study Services
The Sponsor will pay for or provide all study services/activities required as part of your participation in this study. There will be no cost to you.

Items/Services Not Paid for by the Sponsor
Any other medical services provided to you that are not directly required by this study will be billed to you or your insurance company in the usual manner.

DF/HCC FINANCIAL INFORMATION

If you have questions about your insurance coverage, or the items you might be required to pay for, please call financial services for information. The contact information for financial services are:

- Brigham and Women's Hospital: (617) 732-5524 or (617) 732-7485

Will I be paid for taking part in this research?

For taking part in this research, you may be paid up to a total **of $570.** You will receive a payment for each visit you complete. Individual visit payments are made by check and delivered by U.S. Postal mail, typically about 2 weeks after the visit takes place. Study visit payments are as follow:

VISIT	COMPENSATION
Screening Visit	$30
Baseline/Day 0	$85
Weekly Injection Visits (except Week 6 and Week 12)	$25 each (total $250)
Week 6: Mid-point Assessments	$90
Week 12: End of Study Assessments	$90
3-Month Follow up	$25
Total	$570

Who can answer my questions about this research?

You can call us with your questions or concerns. Our telephone numbers are listed below. Ask questions as often as you want.

Dr. Shalender Bhasin is the person in charge of this research study. If you have questions, concerns or complaints about the research, you can call him at 617-525-9150, Monday - Friday 8am - 5pm. You can also call the Clinical Research Coordinator at 617-525-9132, Monday – Friday 8am – 5pm.

If you need to contact a study doctor outside normal business hours, you may call a Brigham and Women's operator 24/7 at 617-732-6660 and ask for Dr. Valderrábano, Dr. Huang, or Dr. Bhasin.

If you have questions about the scheduling of appointments or study visits, call the Clinical Study Coordinator at 617-525-9132.

Contact Information for SEMC:
Dr. Eswara can be reached at 617-789-8181

This research is being overseen by an Institutional Review Board ("IRB"). An IRB is a group of people who perform independent review of research studies. You may talk to them at 855-818-2289, researchquestions@wcgirb.com if:

- You have questions, concerns, or complaints that are not being answered by the research team.
- You are not getting answers from the research team.

- You cannot reach the research team.
- You want to talk to someone else about the research.
- You have questions about your rights as a research subject.

You can also call the St. Elizabeth's Medical Center IRB Office at (617) 789-2804.

Statement of Consent:

Signature of Subject:

I give my consent to take part in this research study and agree to allow my identifiable information to be used and shared as described above.

_____	_____	_____
Subject	Date	Time (optional)

Signature of Study Doctor or Person Obtaining Consent:

- I have explained the research to the study subject.
- I have answered all questions about this research study to the best of my ability.

Adult Participants

To be completed by person obtaining consent:

The consent discussion was initiated on _____ (date).

Signature of individual obtaining consent: _____

Printed name of above: _____

Date: _____

☐ A copy of this signed consent form will be given to the participant.

For Adult Participants

☐ 1) The participant is an adult and provided consent to participate.

☐ 1a) Participant is a non-English speaker and signed the translated Short Form in lieu of English consent document:

As someone who understands both English and the language spoken by the participant, I interpreted and/or witnessed, in the participant's language, the researcher's presentation of the English consent form. The participant was given the opportunity to ask questions.

Signature of Interpreter/Witness: _____

Printed Name of Interpreter/Witness: _____

Date: _____

☐ 1b) Participant is illiterate

The consent form was read to the participant who was given the opportunity to ask questions.

Signature of Witness: _____

Printed Name of Witness: _____

Date: _____

Version: 02/07/2022